6 ANSWER 1 OF 7 MEDLINE
AN 2002300825 MEDLINE
DN 22035333 PubMed ID: 12039861
TI **Human dermal microvascular endothelial** cells form vascular analogs in cultured skin substitutes after grafting to athymic mice.
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NC 5R01GM050509 (NIGMS)
SO FASEB JOURNAL, (2002 Jun) 16 (8) 797-804.
Journal code: 8804484. ISSN: 1530-6860.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200206
ED Entered STN: 20020604
Last Updated on STN: 20020611
Entered Medline: 20020607
AB Cultured skin substitutes (CSS) consisting of autologous fibroblasts and keratinocytes combined with biopolymers are an adjunctive treatment for large excised burns. CSS containing two cell types are limited by anatomical deficiencies, including lack of a vascular plexus, leading to slower vascularization after grafting than split-thickness autograft. To address this limitation, CSS were prepared containing human keratinocytes, fibroblasts, and dermal microvascular endothelial cells (HDMEC) isolated from a single skin sample. After 16 days in culture, control CSS and CSS containing HDMEC (CSS+EC) were grafted to full-thickness wounds in athymic mice. In CSS+EC in vitro, HDMEC persisted in the dermal substitutes and formed multicellular aggregates. One wk after grafting, HDMEC in CSS+EC organized into multicellular structures, some containing lumens. By 4 wk after grafting, HDMEC were found in linear and circular organizations resembling vascular analogs associated with basement membrane deposition. In some cases, colocalization of HDMEC with mouse perivascular cells was observed. The results demonstrate HDMEC **transplantation** in a clinically relevant cultured skin model, persistence of HDMEC after grafting, and HDMEC organization into vascular analogs in vitro and in **vivo**. All cells were derived from the same donor tissue, indicating the feasibility of preparing CSS containing autologous HDMEC for grafting to patients.

ANSWER 2 OF 7 MEDLINE
AN 2001248965 MEDLINE
DN 21201357 PubMed ID: 11304564
TI Engineering and characterization of functional human microvessels in immunodeficient mice.
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NC CA64416 (NCI)
DE13161 (NIDCR)
HL39926 (NHLBI)
SO LABORATORY INVESTIGATION, (2001 Apr) 81 (4) 453-63.
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CY United States
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FS Priority Journals
EM 200105
ED Entered STN: 20010517
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AB SUMMARY: Current model systems used to investigate angiogenesis in **vivo** rely on the interpretation of results obtained with nonhuman endothelial cells. Recent advances in tissue engineering and molecular biology suggest the possibility of engineering human microvessels in **vivo**. Here we show that **human dermal microvascular endothelial** cells (HDMEC) **transplanted** into severe combined immunodeficient (SCID) mice on biodegradable polymer matrices differentiate into functional human microvessels that anastomose with the mouse vasculature. HDMEC were stably transduced with Flag epitope or alkaline phosphatase to confirm the human origin of the microvessels. Endothelial cells appeared dispersed throughout the sponge 1 day after **transplantation**, became organized into empty tubular structures by Day 5, and differentiated into functional microvessels within 7 to 10 days. Human microvessels in SCID mice expressed the physiological markers of angiogenesis: CD31, CD34, vascular cellular adhesion molecule 1 (VCAM-1), and intercellular adhesion molecule 1 (ICAM-1). Human endothelial cells became invested by perivascular smooth muscle alpha-actin-expressing mouse cells 21 days after implantation. This model was used previously to demonstrate that overexpression of the antiapoptotic protein Bcl-2 in HDMEC enhances neovascularization, and that apoptotic disruption of tumor microvessels is associated with apoptosis of surrounding tumor cells. The proposed SCID mouse model of human angiogenesis is ideally suited for the study of the physiology of microvessel development, pathologic neovascular responses such as tumor angiogenesis, and for the development and investigation of strategies designed to enhance the neovascularization of engineered human tissues and organs.

ANSWER 4 OF 7 MEDLINE

AN 2000203765 MEDLINE

DN 20203765 PubMed ID: 10741721

TI Treatment for malignant pleural effusion of human lung adenocarcinoma by inhibition of vascular endothelial growth factor receptor tyrosine kinase phosphorylation.

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NC CA16672 (NCI)
R35-CA42107 (NCI)

SO CLINICAL CANCER RESEARCH, (2000 Mar) 6 (3) 957-65.
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LA English

FS Priority Journals

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AB Malignant pleural effusion (PE) is associated with advanced human lung cancer. We found recently, using a nude mouse model, that vascular endothelial growth factor/vascular permeability factor (VEGF/VPF) is responsible for PE induced by non-small cell human lung carcinoma cells. The purpose of this study was to determine the therapeutic potential of a VEGF/VPF receptor tyrosine kinase phosphorylation inhibitor, PTK 787, against PE formed by human lung adenocarcinoma (PC14PE6) cells. PTK 787 did not affect the in vitro proliferation of PC14PE6 cells, whereas it specifically inhibited proliferation of **human dermal microvascular endothelial** cells stimulated by VEGF/VPF. A specific platelet-derived growth factor receptor tyrosine kinase inhibitor, CGP57148 (used as a control because PTK 787 also inhibits platelet-derived growth factor receptor tyrosine kinases), had no effect on proliferation of PC14PE6 or **human dermal microvascular endothelial** cells. i.v. injection of PC14PE6 cells into nude mice produced lung lesions and a large volume of PE containing a high level of VEGF/VPF. Oral treatment with CGP57148 had no effect on PE or lung metastasis. In contrast, oral treatment with PTK 787 significantly reduced the formation of PE but not the number of lung lesions. Furthermore, treatment with PTK 787 significantly suppressed vascular hyperpermeability of PE-bearing mice but did not affect the VEGF/VPF level in PE or expression of VEGF/VPF protein and mRNA in the lung tumors of PC14PE6 cells in **vivo**. These findings indicate that PTK 787 reduced PE formation mainly by inhibiting vascular permeability, suggesting that this VEGF/VPF receptor tyrosine kinase inhibitor could be useful for the control of malignant PE.